

## REMARKS

The Office Action mailed March 15, 2004, has been carefully considered. The present Amendment is intended to be a complete response thereto and to place the case in condition for allowance.

Claims 1 and 6-27 are pending. Claims 2-5 have been cancelled. Claims 7-8, 13-18, and 20-27 have been withdrawn from consideration as being drawn to non-elected inventions. Claims 1, 9-11, and 19 have been amended. Support for amended claim 1 is found, *inter alia*, in the specification on page 6, Table 1, and claims 2-5 as originally filed. Claims 9-11 and 19 have been amended to correct minor errors and to be in correspondence with amended claim 1.

### THE CLAIMS ARE DEFINITE

Claims 9-11 and 19 stand rejected under 35 U.S.C. § 112, second paragraph, as being indefinite. The Examiner alleges that the abbreviation mcg/L is not commonly used in the art. Application has amended the present application to read micrograms/L. Applicant respectfully submits that mcg/L is well understood in the art to be an abbreviation for micrograms/L. A quick search of the USPTO database yields 153 patents that use the abbreviation mcg for microgram. Most recently, U.S. Patent No. 6,765,002 uses the abbreviation "mcg" or "µg" interchangeably for microgram. Therefore, the abbreviation mcg is recognized in the art as an abbreviation for microgram.

### THE CLAIMS ARE NOT ANTICIPATED

Claims 1-5 stand rejected under 35 U.S.C. § 102(b) as being anticipated by Fukuse et al. (1996), *Transplantation*, 62:1212-1217. Applicant respectfully traverses the rejection.

To anticipate a claim, the reference must teach every element of the claim. *See* MPEP § 2131. "A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987). "The identical invention must be shown in as complete detail as is contained in the ... claim." *Richardson v. Suzuki Motor Co.*, 868 F.2d 1226, 1236, 9 USPQ2d 1913, 1920 (Fed. Cir. 1989). The elements must be arranged as required by the claim, but this is not an *ipsissimis verbis* test, i.e., identity of terminology is not required. *In re Bond*, 910 F.2d 831, 15 USPQ2d 1566 (Fed. Cir. 1990).

Fukuse et al. fail to disclose every element of the claimed invention. Particularly, the reference fails to disclose "100-5000 micrograms/L of prostaglandin E1," as recited by currently amended claim 1. Fukuse et al. disclose the use of 25 µg/Kg of prostaglandin E1 (PGE1). However, the present invention uses 100-5000 micrograms/L regardless of the weight of the animal. The disclosure of Fukuse et al. and the present invention differ in that the amount of PGE1 used by Fukuse et al. is based on the animal weight, while the amount used by the invention is based on the amount of solution. Therefore, because Fukuse et al. fail to disclose the particular concentration of the present invention, it cannot anticipate the invention within the meaning of 35 U.S.C. § 102. Accordingly, Applicant respectfully requests reconsideration and withdrawal of the rejection.

#### THE CLAIMS ARE NOT OBVIOUS

Claims 1-6, 9-12 and 19 stand rejected under 35 U.S.C. § 103(a) as being obvious over 1) Polyak et al. (2000), *Transplantation* 69:249-258, or Polyak et al. (1999), *Transplantation*

*Proceedings* 31:2091-2093, in view of Stern et al. (U.S. Patent No. 5,552,267); and 2) Osgood (U.S. Patent No. 5,712,084) or Strasberg et al. (U.S. Patent No. 5,200,398), in view of Stern et al. and Vargas (1995), *Journal of American College of Surgeons* 180:713-717. Applicant respectfully traverses the rejection.

To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations. *See* MPEP 2143.

The Examiner alleges that 1) the Polyak et al. references disclose the use of 500 µg/L of PGE1 in a Belzer solution; 2) Stern et al. disclose a perfusion solution containing NAC and nitroglycerin (NTG); 3) Osgood discloses a Belzer solutions for kidney perfusion; and 4) Vargas et al. disclose a kidney perfusion solution containing PGE1. Accordingly, the Examiner concludes that "it is *prima facie* obvious to combine two or more ingredients each of which is taught by the prior art to be useful for the same purpose in order to form a third composition which is useful for the same purpose." Even assuming that the Examiner has produced a *prima facie* case of obviousness (which Applicant denies), Applicant's present invention is supported by the unexpected result that the combination of 100-5000 micrograms/L of prostaglandin, a nitric oxide donor, and a glutathione-forming agent produces synergistic effects that are unexpected from the teachings of the prior art. Applicant submits herewith an Declaration under 37 C.F.R. § 1.132 showing unexpected result. In summary, the data presented in the Declaration shows that post-transplant serum creatine decreased unexpectedly when the cold storage solution

contains 1000 microgram/mL of prostaglandin (PGE1), 10 mg/L of nitroglycerin (NTG), and 0.2 mg/L of N-acetylcysteine (NAC). Addition of PGE1, NTG, or NAC individually to the control solution did not significantly improve post-transplant function (decrease in serum creatine). Thus, one of ordinary skill in the art would have concluded that the combination of all three components (PGE1, NTG, and NAC) in the cold storage solution would produce the same result, i.e. insignificant improvement in post-transplant function. However, Applicant has discovered that when all three components are added together, the improvement in post-transplant function is drastic, unexpected, and greater than the sum of the individual components. Because no one component individually demonstrated a substantial improvement compared to the control, one of ordinary skill in the art would not expect the synergistic improvement discovered by Applicant. Further, this unexpected result is neither taught, suggested, nor contemplated by the cited references. Therefore, because Applicant's invention is support by unexpected result, Applicant respectfully requests reconsideration and withdrawal of the rejection.

## CONCLUSION

Applicant has responded to the Office Action mailed March 15, 2004. A Petition for Revival, a Petition for a three-month extension of time, and fees therefore are filed herewith. All pending claims are now believed to be allowable and favorable action is respectfully requested.

In the event that there are any questions relating to this Amendment or to the application in general, it would be appreciated if the examiner would telephone the undersigned attorney concerning such questions so that the prosecution of this application may be expedited.

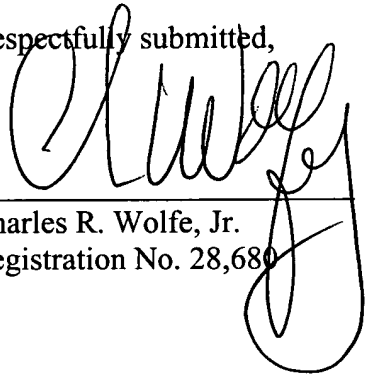
Please charge any shortage or credit any overpayment of fees to BLANK ROME LLP, Deposit Account No. 23-2185 (122790-00101). In the event that a petition for an extension of time is required to be submitted herewith and in the event that a separate petition does not accompany this response, applicant hereby petitions under 37 C.F.R. 1.136(a) for an extension of time for as many months as are required to render this submission timely.

Any fees due are authorized above.

Date: May 13, 2005

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Respectfully submitted,

  
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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re the Application of:

Polyak et al.

Serial No.: 09/976,804

Filed: October 12, 2001

For: COLD STORAGE SOLUTION FOR  
ORGAN AND BIOLOGICAL TISSUE  
PRESERVATION



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) Examiner: S. E. Saucier

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) Group Art Unit: 1651

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) Atty. Dkt. 122790-00101.1  
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DECLARATION OF MAXIMILIAN POLYAK UNDER 37 C.F.R. § 1.132

Commissioner of Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

Sir:

I, Maximilian Polyak, one of the named inventors of the above-identified patent application, declare as follows.

1. The experiments and graphs described herein were prepared under my supervision and control in order to demonstrate that the present invention is supported by an unexpected result, not taught, suggested, nor contemplated by the prior art.

2. The experiments were performed as follows:

Sprague-Dawley rat kidneys were recovered in the normal fashion and were exsanguinated and cooled to 4°C. Experimental components were added to the solution to test for improvements in post-transplant function (indicated by serum creatinine levels). Four different solutions were prepared for comparison according to Table 1. According to Table 1, the control VIASP solution contains only Viaspan solution; the PEG100 solution contains

Viaspan and 1000 µg/L prostaglandin E1; the NTG10 solution contains Viaspan and 10 mg/L nitroglycerin; the NAC solution contains Viaspan and 0.2 mg/L N-acetylcystein; and the COMB solution contains Viaspan, 1000 µg/L prostaglandin E1, 10 mg/L nitroglycerin, and 0.2 mg/L N-acetylcystein. Kidneys were preserved under static conditions for 24 hours with the respective solutions, and transplanted into recipient animals. Post-transplant serum creatinine (S. CREAT) was measured hourly for 6 hours.

TABLE 1

	VIASP	PGE1000	NTG10	NAC	COMB
Viaspan	+	+	+	+	+
Prostaglandin E1 (1000 µg/L)	-	+	-	-	+
Nitroglycerin (10 mg/L)	-	-	+	-	+
N-Acetylcystein (0.2 mg/L)	-	-	-	+	+

3. The result of the experiment is depicted in Figure 1. Minimal, but statistically insignificant improvements in post-transplant function were observed with prostaglandin E1, nitroglycerin, or N-acetylcystein individually when compared to the control. From this observation, one of ordinary skill in the art would not have expected significant improvement when prostaglandin E1, nitroglycerin, and N-acetylcystein are used together (the COMB solution). However, dramatic improvement was observed with the cumulative effect on post-transplant function of the COMB solution when compared to the control. Because no one individual component demonstrated a substantial improvement compared to the control, a synergistic improvement when all components were added is not expected.

4. In summary, the experiment presented shows an unexpected result that would not have been obvious to one of ordinary skill in the art by reviewing the prior art.

5. I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under 18 U.S.C. § 1001, and that such willful false statements may jeopardize the validity of the application of any patent issued thereon.

Date:

5/12/05



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PGE1, NTG, and NAC (cold storage)

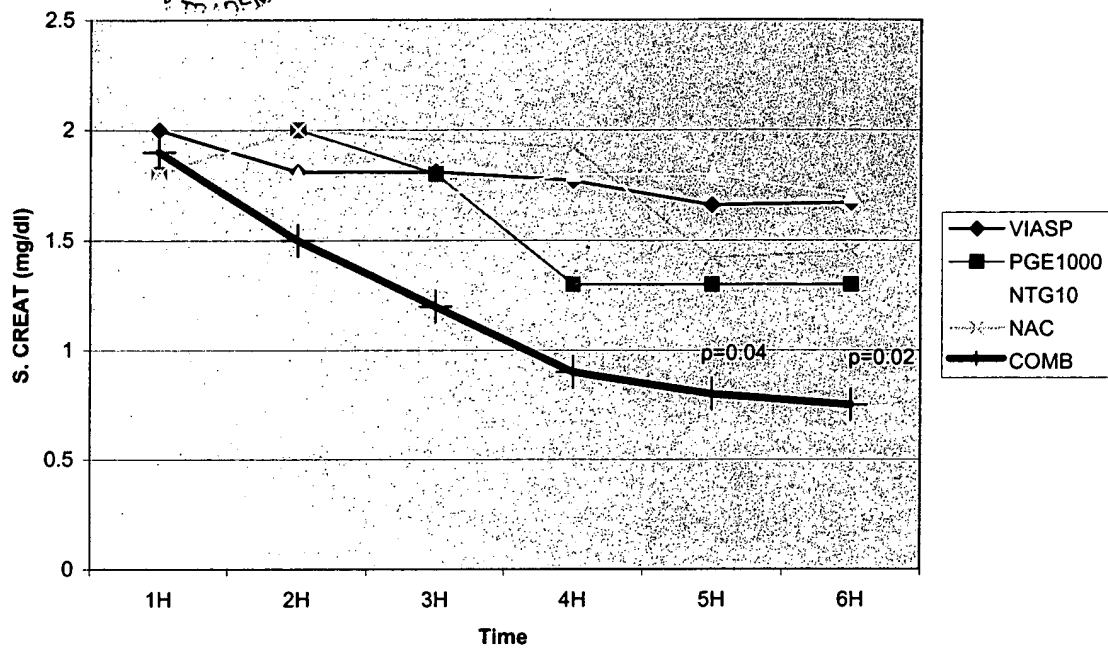


FIGURE 1

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